

WHAT IS CLAIMED IS:

1 1. A method of correlating gene and protein expression in a biological
2 sample, the method comprising the steps of:
3 a) obtaining the biological sample ;
4 b) generating a gene expression profile of the sample, thereby identifying
5 an mRNA expressed in the sample;
6 c) identifying a physio-chemical property of a polypeptide encoded by the
7 mRNA;
8 d) fractionating polypeptides in the sample on the basis of the physio-
9 chemical property and;
10 (e) identifying the polypeptide encoded by the mRNA from among the
11 fractionated proteins, wherein the identified polypeptide comprises the physio-chemical
12 property;
13 thereby correlating gene and protein expression in the sample.

1 2. The method of claim 1, wherein the biological sample comprises a
2 cell lysate from a healthy cell.

1 3. The method of claim 1, wherein the biological sample comprises a
2 cell lysate from a pathological cell.

1 4. The method of claim 1, wherein the biological sample comprises a
2 cell lysate from a cell contacted by a toxic compound.

1 5. The method of claim 1, wherein the biological sample comprises a
2 cell lysate from a cell of a subject who respond to a drug treatment or a subject who does
3 not respond to a drug treatment.

1 6. The method of claim 1, wherein the biological sample comprises a
2 cell lysate from a cell exposed to heat, cold, or radiation.

1 7. The method of claim 1, wherein the biological sample comprises a
2 human cell.

1 8. The method of claim 1, wherein the step of generating the gene
2 expression profile comprises identifying expressed mRNA with an EST array.

1 9. The method of claim 1, wherein the step of generating the gene
2 expression profile comprises identifying expressed mRNA with an oligonucleotide array.

1 10. The method of claim 1, wherein the step of generating the gene
2 expression profile comprises identifying expressed mRNA with an mRNA array.

1 11. The method of claim 1, wherein the mRNA is differentially
2 expressed in two biological samples.

1 12. The method of claim 11, wherein the two biological samples are
2 derived from a normal cell and a pathologic cell.

1 13. The method of claim 12, wherein the pathologic cell is a cancer
2 cell.

1 14. The method of claim 11, wherein the two biological samples are
2 derived from a healthy cell and a cell exposed to a toxic compound.

1 15. The method of claim 1, wherein the step of identifying the physio-
2 chemical property of the polypeptide encoded by the mRNA further comprises
3 identifying a plurality of physio-chemical properties.

1 16. The method of claim 1, wherein the step of identifying a physio-
2 chemical property comprises predicting the masses of proteolytic fragments generated by
3 the polypeptide encoded by the mRNA upon degradation of the polypeptide by a selected
4 proteolytic agent, and the step of identifying the polypeptide encoded by the mRNA
5 comprises subjecting polypeptides in the sample to degradation by the agent and
6 identifying actual proteolytic fragments in the sample having masses that correspond to
7 the masses of the predicted fragments.

1 17. The method of claim 1, wherein the physio-chemical property is
2 selected from the group consisting of: amino acid sequence, molecular weight, iso-
3 electric point, hydrophobicity, hydrophilicity, glycosylation, phosphorylation, epitope
4 sequence, ligand binding sequence, charge at a specified pH, and metal chelate binding.

1 18. The method of claim 1, wherein the step of fractionating the
2 polypeptides in the sample comprises 2D-gel electrophoresis.

1 19. The method of claim 1, wherein the step of fractionating the
2 polypeptides in the sample comprises mass spectrometry.

1 20. The method of claim 1, wherein the step of fractionating the
2 polypeptides in the sample comprises surface enhanced laser desorption ionization,
3 wherein the surface enhanced laser desorption ionization comprises fractionating by
4 affinity retention on solid phase-bound adsorbent followed by fractionating retained
5 polypeptides from the solid phase by gas phase ion spectrometry.

1 21. The method of claim 20, wherein the adsorbent is selected to have
2 affinity for polypeptides possessing at least one physio-chemical property selected from
3 the group consisting of: amino acid sequence, molecular weight, iso-electric point,
4 hydrophobicity, hydrophilicity, glycosylation, phosphorylation, epitope sequence, ligand
5 binding sequence, charge at a specified pH, and metal chelate binding.

1 22. The method of claim 1, wherein the step of identifying the
2 polypeptide comprises selecting a polypeptide from among the fractionated polypeptides,
3 which selected polypeptide comprises the physio-chemical property, identifying the
4 selected polypeptide and correlating the identity of the selected polypeptide with the
5 polypeptide encoded by the mRNA.

1 ~~23.~~ A method of correlating gene and protein expression in a biological
2 sample, the method comprising the steps of:

3 a) obtaining a biological sample;

4 b) generating a gene expression profile of the sample using a nucleic acid
5 array, thereby identifying an mRNA expressed in the sample;

6 c) identifying a physio-chemical property of a polypeptide encoded by the
7 mRNA;

8 d) fractionating polypeptides in the sample on the basis of the physio-
9 chemical property, using mass spectrometry and;

10 (e) identifying the polypeptide encoded by the mRNA from among the
11 fractionated proteins, wherein the identified polypeptide comprises the physio-chemical
12 property;

13 thereby correlating gene and protein expression in the cell.

1 24. The method of claim 23, wherein the step of generating the gene
2 expression profile comprises identifying expressed mRNA with an EST array.

1 25. The method of claim 23, wherein the step of generating the gene
2 expression profile comprises identifying expressed mRNA with an oligonucleotide array.

1 26. The method of claim 23, wherein the step of generating the gene
2 expression profile comprises identifying expressed mRNA with an mRNA array.

1 27. The method of claim 23, wherein the step of identifying the
2 polypeptide encoded by the mRNA comprises fractionating polypeptides in the sample by
3 surface enhanced laser desorption ionization, wherein the surface enhanced laser
4 desorption ionization comprises fractionating by affinity retention on solid phase-bound
5 adsorbent followed by fractionating retained polypeptides from the solid phase by gas
6 phase ion spectrometry.

1 28. A method of correlating gene and protein expression in a biological
2 sample, the method comprising the steps of:

3 a) obtaining a biological sample;
4 b) generating a gene expression profile of the sample using an
5 oligonucleotide array, thereby identifying an mRNA expressed in the sample;

6 c) identifying a physio-chemical property of a polypeptide encoded by the
7 mRNA;

8 d) fractionating polypeptides in the sample on the basis of the physio-
9 chemical property with surface enhanced laser desorption ionization, wherein the surface
10 enhanced laser desorption ionization comprises fractionating by affinity retention on solid
11 phase-bound adsorbent followed by fractionating retained polypeptides from the solid
12 phase by gas phase ion spectrometry; and

13 e) identifying the polypeptide encoded by the mRNA from among the
14 fractionated proteins, wherein the identified polypeptide comprises the physio-chemical
15 property;

16 thereby correlating gene and protein expression in the cell.

1 29. The method of claim 28, wherein the adsorbent is selected to have
2 affinity for polypeptides possessing at least one physio-chemical property selected from

3 the group consisting of: amino acid sequence, molecular weight, iso-electric point,
4 hydrophobicity, hydrophilicity, glycosylation, phosphorylation, epitope sequence, ligand
5 binding sequence, charge at a specified pH, and metal chelate binding.

1 30. The method of claim 28, wherein the step of identifying the physio-
2 chemical property comprises predicting the masses of proteolytic fragments generated by
3 the polypeptide encoded by the mRNA upon degradation of the polypeptide by a selected
4 proteolytic agent, and the step of identifying the polypeptide encoded by the mRNA
5 comprises subjecting polypeptides in the sample to degradation by the agent and
6 identifying actual proteolytic fragments in the sample having masses that correspond to
7 the masses of the predicted fragments.

10076967-021502